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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,457	06/19/2006	Kazunori Nakamura	292672US0X PCT	8983
22850 7590 09/15/2008 OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			EXAMINER WOOLWINE, SAMUEL C	
			ART UNIT	PAPER NUMBER
			1637	
			NOTIFICATION DATE	DELIVERY MODE
			09/15/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/583,457	Applicant(s) NAKAMURA ET AL.	
	Examiner SAMUEL WOOLWINE	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 July 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) 2-5 and 7-9 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,6,10 and 11 is/are rejected.
- 7) ☒ Claim(s) 1,6,10 and 11 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>06/19/2006;05/07/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1, 6, 10 and 11, in the reply filed on 07/03/2008 is acknowledged.

Claims 2-5 and 7-9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 07/03/2008.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Objections

Claims 1, 6, 10 and 11 are objected to because of the following informalities: the claims are not in proper form. MPEP 608.01(m) sets forth:

"Each claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations. See *Fressola v. Manbeck*, 36 USPQ2d 1211 (D.D.C. 1995)."

Claim 1 contains extra periods at the end of sections A) and B). Claim 6 contains an extra period at the end of the second section. Claim 11 contains extra periods used in the enumeration of sections (i.e. 1., 2., 3.) and at the end of sub-sections 5) and 15).

MPEP 608.01(m) also sets forth:

"Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation, 37 CFR 1.75(i). There may be plural indentations to further segregate subcombinations or related steps."

Claim 1 contains several layers of descriptive elements and should be structured to set each layer apart with appropriate indentations.

Claim 10 depends from claims 1 or 6 and is therefore objected to for the same reasons.

Appropriate correction is required.

Claim Interpretation

Claim 1 is a lengthy claim for a composition of matter that incorporates several recitations of intended use. Only the actual structure of the claimed composition will be considered.

Claim 1 will be interpreted as a mixture or reaction solution comprising one or more target nucleic acid probes and one or more internal standard nucleic acids and, optionally, one or more internal standard nucleic acid probes, wherein:

1) the target nucleic acid probe is a single-stranded oligonucleotide labeled with one or more fluorescent dyes on either an end portion and/or a base moiety and/or a sugar moiety and/or a phosphate moiety;

2) a fluorescent character of the target nucleic acid probe changes upon hybridization with the target nucleic acid and/or the internal standard nucleic acid;

3) the target nucleic acid probe is capable of hybridizing with the target nucleic acid and with the internal standard nucleic acid;

4) the amount of change of a fluorescent character of the target nucleic acid probe upon hybridization of the probe to the target nucleic acid is different than the amount of change of the fluorescent character of the target nucleic acid probe upon hybridization of the probe to the internal standard nucleic acid;

5) the internal standard nucleic acid has a structure different than the target nucleic acid corresponding to the target nucleic acid probe;

6) the optional internal standard nucleic acid probe has characteristics 1) through 4) above, and wherein the fluorescent labeling portion and character of the optional internal standard nucleic acid probe are different from the fluorescent labeling portion and character of the target nucleic acid probe.

The term "fluorescent labeling portion" of item 6) will be broadly interpreted as encompassing a position of the label, the sequence that is labeled (e.g. the nucleotide that is labeled), and/or the label molecule itself. The "character" of the fluorescent label will be broadly interpreted as a structure, absorption/emission maximum, absorption/emission minimum, absorption/emission spectrum, absorption/emission intensity, fluorescence lifetime, fluorescence polarization, etc.

With regard to claim 6, the last portion of the claim reads (underscore added): "The base sequence of a portion of said internal standard nucleic acid hybridizing with said nucleic acid probe is different in part from the base sequence of a portion of a nucleic acid hybridizing with said nucleic acid probe". A nucleic acid will be interpreted as "a target nucleic acid".

Claim 11 will be construed as set forth in the rejection under 35 U.S.C. 112, 2nd paragraph below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With regard to claim 6, the recitation "Said nucleic acid probe..." lacks antecedent basis in the claim. The claim preamble recites "comprises a pair of the below nucleic acid and the below internal standard nucleic acid". It is presumed this should read "comprises a pair of the below nucleic acid probe and the below internal standard nucleic acid". Appropriate correction is required.

Claim 11 is indefinite for the following reasons:

(I) The claim recites "A target nucleic acid probe or a doubly-labeled nucleic acid probe, wherein said target nucleic acid probe or doubly-labeled nucleic acid probe is described above...". This is indefinite because it cannot be determined what "described above" refers to (a preceding claim? specification?) or what limitations if any are required by such reference.

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(II) The claim continues "and has at least any one of the below structures...".

This is indefinite because it cannot be determined whether "one of the below structures" refers to elements enumerated "1.", "2." or "3." as a whole (i.e. including all the sub-elements enumerated under that element), or whether "one of the below structures" refers to any one of the sub-elements enumerated as "1)" through "18)".

(III) The sub-element 15) recites: "a novel mixture according to claim 1 or 5, wherein, in any one of the above 1 to 14...". This is indefinite because it causes confusion as to whether this claim is a claim for a nucleic acid probe, as recited at the beginning of the claim, or a claim for a "novel mixture" comprising such probe.

For purposes of examination over the prior art, claim 11 will be construed as follows: A target nucleic acid probe, which is optionally doubly-labeled, wherein in the case that the probe is doubly-labeled, the probe has at least any one of the characteristics recited in sub-elements 6) through 18), and wherein in the case that the probe is not doubly-labeled, the probe has at least any one of the characteristics recited in sub-elements 1) through 5) or 11) through 18). The phrase "a novel mixture according to claim 1 or 5" recited in sub-element 15) will be given no patentable weight.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Nazarenko et al (US 2003/0165859, prior art of record).

The composition of claim 1 is construed to comprise one or more nucleic acid probes and one or more internal standard nucleic acids. The phrase "or further one or two or more below internal standard nucleic acid probes" is construed as optional; hence the composition of claim 1 minimally requires a composition comprising one nucleic acid probe and one internal standard nucleic acid. Although claim 1 recites limitations regarding how the nucleic acid probe would behave in the presence of a target, these limitations are not structurally distinguishing since there is no particular target specified by the claim. Furthermore, the "target" need not be found in the prior art, but merely the nucleic acid probe and the internal standard nucleic acid. This being the case, claim 1 is anticipated by the disclosure of Nazarenko et al (US 2003/0165859, published 4 September 2003). Nazarenko teaches a nucleic acid probe and internal standard nucleic acid, for example in figure 35:

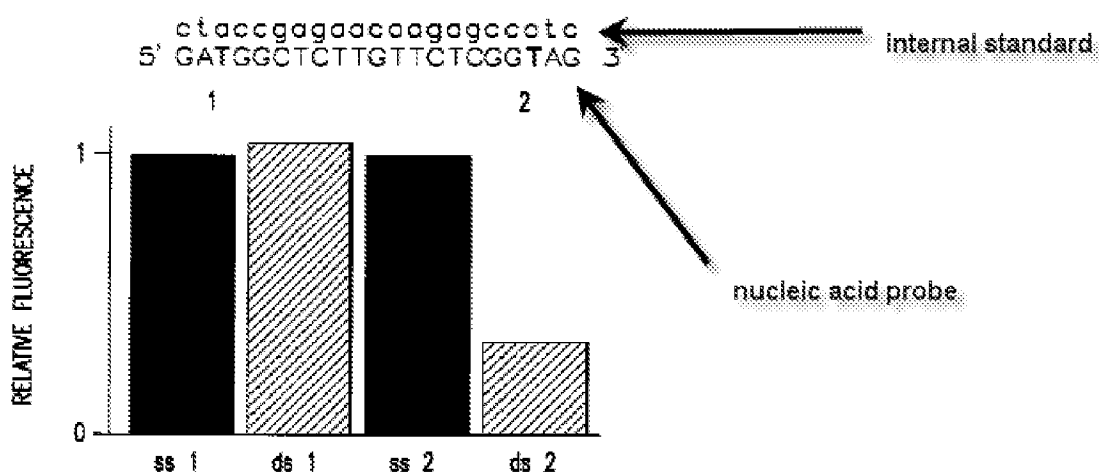


FIG.35

From the discussion in paragraph [0216], it is clear that Nazarenko formed a mixture comprising both of these molecules, and it is also clear that, in the case of the probe labeled at position 2, there was significant change in fluorescence upon hybridization of the probe to the internal standard. Although Nazarenko does not teach using the nucleic acid molecule shown in lower case in figure 35 as an internal standard, it is structurally indistinguishable from the claimed internal standard, since it is capable of hybridizing with and changing a fluorescence characteristic of the nucleic acid probe. Furthermore, a nucleic acid target could be made such that the nucleic acid probe would undergo a different degree of fluorescence change upon hybridization to said target, since it would appear from the claim language and from the specification (e.g. figure 1, bottom panel) that all that would be required would be to synthesize a target nucleic acid that would create a mismatch relative to the internal standard gene. However, as explained above, it is not the target which must be found in the prior art, but only the claimed mixture which comprises a probe and an internal standard. This being the case, the pair of nucleic acids from Nazarenko's figure 35 shown above meets all the structural limitations required by claim 1.

With regard to the requirement that the internal standard nucleic acid have a structure that is different than the target nucleic acid, it is again noted that the claimed composition does not itself comprise a target nucleic acid, and no particular target nucleic acid is recited in the claim. Therefore, this limitation does not structurally distinguish over the pair of nucleic acids taught by Nazarenko, which meet the limitations of the claimed target nucleic acid probe and internal standard nucleic acid.

With regard to claim 6, this claim is construed to be a mixture comprising a nucleic acid probe and an internal standard nucleic acid. The only apparent differences between claim 1 and claim 6 are that claim 6 does not recite the optional internal standard nucleic acid probe of claim 1, claim 6 does not specify the location of the fluorescent labels, and claim 6 includes an additional requirement that the base sequence of the internal standard nucleic acid is different than the base sequence of a target nucleic acid. An additional difference is that claim 6 includes the proviso that, in the case when said nucleic acid probe is plural, the fluorescent dyes labeled on said plural nucleic acid probes each are different. Otherwise, the composition of claim 6 appears to be the same as the composition of claim 1 in terms of the functional properties recited. With regard to the noted proviso regarding the case where the nucleic acid probe is plural, it is noted that the claim does not require a plurality of different nucleic acid probes. Therefore, in the situation where the prior art teaches a single species of nucleic acid probe, this limitation need not be considered.

As was the case for claim 1, the composition taught by Nazarenko comprising the pair of nucleic acids shown in figure 35 above meets the compositional and structural limitations of claim 6.

With regard to the requirement that the internal standard nucleic acid have a base sequence that is different than the target nucleic acid, it is again noted that the claimed composition does not itself comprise a target nucleic acid, and no particular target nucleic acid is recited in the claim. Therefore, this limitation does not structurally

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distinguish over the pair of nucleic acids taught by Nazarenko, which meet the limitations of the claimed target nucleic acid probe and internal standard nucleic acid.

With regard to claim 11, as discussed under the rejection of claim 11 under 35 U.S.C. 112, 2nd paragraph above, the claim can be construed as being a target nucleic acid probe having any one of the features recited in sub-elements 1) through 5) or 11) through 18).

Hence, the target nucleic acid probe taught by Nazarenko meets the limitations of claim 11 for at least the case of a target nucleic acid probe as described by sub-element 1): "said structure has a portion not complementary to a target nucleic acid".

With regard to the requirement that the target nucleic acid probe has a portion not complementary to a target nucleic acid, it is again noted that the claimed composition does not itself comprise a target nucleic acid, and no particular target nucleic acid is recited in the claim. Therefore, this limitation does not structurally distinguish over the target nucleic acid probe taught by Nazarenko.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nazarenko et al (US 2003/0165859, prior art of record).

The composition taught by Nazarenko meeting the limitations of claims 1 and 6 has been discussed. It is also noted that Nazarenko also teaches kits (see paragraph [0082]).

Nazarenko does not explicitly teach to place the particular mixture of probe and internal standard nucleic acid as shown in figure 35 into a kit.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to package the mixture comprising the pair of nucleic acid shown in Nazarenko's figure 35 in the form of a kit since Nazarenko teaches kits for the purpose of detecting nucleic acid, and the mixture of the two nucleic acids shown in figure 35 would have served as a positive control for an assay designed to use the labeled nucleic acid as a probe for detecting a target comprising the sequence of the other nucleic acid (i.e. the unlabeled strand) shown in figure 35.

Conclusion

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL WOOLWINE whose telephone number is (571)272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samuel Woolwine/
Examiner, Art Unit 1637